Allergy Abstracts

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Asthma and Hay Fever

Preliminary Report on Adrenocorticotropic Hormone (ACTH) in Asthma. Rose, B., Pare, J. A. P., Pump, K., and Stanford, R. C.: Canad. M. A. J. **62**: 6, 1950.

Six patients with severe asthma of several years' duration were treated with adrenocorticotropic hormone (ACTH), 75 to 150 mg. per day for from 4 to 6 days. The drug was administered intramuscularly; the total daily dose was apportioned and given every 6 hours. Four patients experienced complete remission within 48 hours and substantial improvement was noted in the remaining 2. Complete remission lasted for 1 month or less. Symptoms recurred with their initial severity within 2 weeks. Cutaneous reactions were not affected. Urinary histamine was decreased markedly while ACTH was being administered. It is suggested that part of the activity of ACTH in asthmatics may be due to restoration of the histidine-histamine balance in the lung. K.

Respiratory Allergy Due to Fungi. Walton, C. H. A.: Canad. M. A. J. **60**: 272, 1949.

Among a group of 275 asthmatics seen consecutively over an 18-month period, 36 per cent showed positive cutaneous responses to 1:1000 dilutions of fungus extracts. Thirty-two per cent of the entire group evidenced clinical sensitivity to fungi. The ages of these patients ranged from infancy to 70 years, the majority being between 6 and 40 years of age. Three-fifths lived in urban areas. Of the 88 mold reactors, 77 showed positive skin reactions to Alternaria, Hormodendrum, or Helminthosporium. Fifty-nine appeared to be clinically sensitive to these molds. Rusts and smuts were responsible for skin reactions in 43 cases, but appeared to be of clinical importance in only 17. "Nonseasonal fungi," including yeasts, Penicillium, Lycopodium, Mucor, Monilia, Rhizopus, and Aspergillus, produced positive cutaneous reactions in 67 of the asthmatics and were considered clinically important in 46 cases. The author considers fungal spores to be of major importance as a cause of allergic symptoms in Manitoba, Canada. K.

Persistent Cough and Bronchospasm Due to Exposure to Fumes From Range Oil. A New Clinical Syndrome. Brown, E. A.: Ann. Allergy **7**: 756, 1949.

A syndrome of persistent cough and expiratory wheezing lasting from early fall to late spring, and due to inhalation of range oil fumes, is described. The irritating, incompletely combusted aldehydes emanating from faulty ranges appears to be the cause of this syndrome. W.

Determination of the Specific Gravity of Ragweed Pollen and Conversion of Gravity Sample Counts to Volumetric Incidence. Crawford, J. H.: U. S. Pub. Health Rep. **64**: 1195, 1949.

Using improved methods, the writer reinvestigated the specific gravity of ragweed pollen. Pollens generally vary in specific gravity from 0.50 to 1.00. The low specific gravity of pollen would suggest that pollen grains are made up of a spongelike mass. The specific gravity of ragweed pollen was found to be 11.3. This indicated that the pollen grain is more dense than previously postulated. The rate of fall for the ragweed pollen was computed at 0.525 feet per second. The revised Scheppegrell-Dahl formula herein presented now reads $n - 5.53$ N, where n denotes the approximate number of pollen grains per cubic yard of air and N represents the number of pollen grains per square centimeter of exposed slide surface. H.

Preliminary Report on Atmospheric Pollen Studies. Wiley, J. S., and Tarzwell, C. M.: Supplement to the Proceedings of the Northeastern States Weed Control Conference. Jan., 1950, p. 34.

A ragweed pollen survey was conducted in the Cincinnati area during the 1949 season. Standard pollen shelters were employed at thirteen stations. Various studies were done to check the efficacy of gravity sampling for the quantitative determination of atmospheric ragweed pollen. It was found that counts at two points, 10 feet apart, were similar. Glycerine jelly-coated slides showed slightly greater counts and appeared easier to count than petrolatum-coated slides, but the former were more easily ruined by driving rains. Slides exposed on the bottom disc of the standard shelter showed counts only slightly greater than those in the slide holder. Standard slides and inverted slides were exposed simultaneously in the same holders in standard instruments. The standard slides collected about twice as much pollen as the inverted slides. However, appreciable counts were obtained on the inverted slides, indicating that sedimentation of pollen is not the sole determinant in gravity slide counts. There seemed to be fair direct correlation between gravity counts with elevation above ground level and wind velocity and an inverse correlation with rainfall. Correlations could not be made with other meteorologic factors.

Gravity slide counts on six days bore no constant ratio to counts obtained with three different volumetric sampling devices. Due to this discrepancy it was concluded that gravity counts should not be converted to volumetric counts. It was suggested that wind and air currents are important factors in the amount of pollen deposited on gravity slides. B. S.

Wood Dust as Inhalant Allergen. Bronchial Asthma Caused by Wood. Ordman, D.: South African M. J. **23**: 973, 1949.

A cabinetmaker, aged 29 years, who had been working with woods since the age of 14, developed asthma when he began to handle Kejaat wood. Kejaat is a brown, durable wood which grows in the Transvaal. Mahogany, walnut, teak, and pine woods produced no symptoms. Desensitization with Kejaat wood extract administered intracutaneously proved successful. Intracutaneous tests with an extract of Kejaat were positive. H.

Incidence of Bronchial Asthma in General Practice. Kurtz, I. M.: New York State J. Med. **50**: 1247, 1950.

An analysis was made of 1,043 cases of bronchial asthma gathered from the Medical Care Program of the New York City Department of Welfare. This series included 610 females and 433 males. The number of cases was highest during the first decade of life and then declined between the ages of 11 and 30. The curve rose again between the fifth and seventh decades and declined sharply during the eighth and ninth decades. During the first decade, the incidence of asthma was higher among males than among females, the ratio being about 3 to 2. Between the ages of 20 and 50, 4 times as many females as males had asthma. This finding suggests that hormonal factors may play an important role in the pathogenesis of bronchial asthma. Among the various conditions found to coexist with bronchial asthma, cardiac diseases were the most common, occurring in 12 per cent of the cases. B. S.

Dermatology

Sensitivity to Furacin. Richter, I. H., and Manocchio, A. C.: New York State J. Med. **49**: 2325, 1949.

Thirty patients with varicose ulcers were treated from one to four weeks by the local applications of Furacin Soluble Dressing. Three patients, two of whom were atopic, developed a generalized eruption characteristic of the delayed, induced type of contact dermatitis. C.

A Comparison of Paradione and Tridione in the Treatment of Epilepsy. Davis, J. P., and Lennox, W. G.: J. Pediat. **34**: 273, 1949.

The therapeutic and side effects of Paradione and Tridione were analyzed in over 100 patients suffering from epilepsy. Fifteen per cent of patients receiving Paradione and 21 per cent receiving Tridione developed generalized rashes. Of the 11 patients who developed eruptions from Paradione, 5 had a morbiliform rash, 3 developed urticaria, and 3 showed eczematoid, hemorrhagic, or acneiform rashes. Of the 15 patients taking Tridione, 12 showed a morbiliform rash, 2 had an acneiform rash, and 1 had an eczematoid rash. J. S.

Effects of Various Modes of Administration of Pyribenzamine on the Histamine Wheal and Epidermal Sensitivity Reactions. Peck, S. M., Finkler, B., Gernsheim, G., and Michelferder, T.: J. Invest. Dermat. **14**: 177, 1950.

Histamine wheals and flares were diminished by previous oral administration, local subcutaneous injection, or by iontophoresis of Pyribenzamine. The preparation of sites with Pyribenzamine Ointment had little effect on the histamine reaction. On patients with known contact sensitivities, patch tests reactions were not influenced by the oral administration, the local subcutaneous injection, or topical application of Pyribenzamine. In these cases, however, the patch test reactions were reduced by the preparation of sites with Pyribenzamine applied iontophoretically. Novocain applied locally by iontophoresis or by local injection had no effect on the patch test reactions.

Using a fluorophotometric method for determining the presence in the urine of compounds containing the pyridine radical, Pyribenzamine could not be detected within nine hours after a large amount of ointment was rubbed into normal skin. However, following the application of Pyribenzamine Ointment to areas of dermatitis, appreciable amounts of the drug were found in the urine. Pyribenzamine, when applied by iontophoresis over normal areas of skin, was detectable in the urine. The most important single factor in antihistaminic therapy is the introduction of the drug in proper concentration at the site where the clinical manifestations are present. Urticarial reactions, therefore, are best treated by the oral or parenteral routes. Since topical applications of antihistaminics readily find their way through damaged epidermis, this method is

the route of choice in reactions of epidermal sensitivity. It is suggested that iontophoresis of Pyribenzamine be used as a means of protection of normal skin against future epidermal sensitivity reactions. B. S.

Fixed Drug Eruption From Tetraethylthiuram Disulfide (Antabuse). Lewis, H. M., and Bremers, H. H.: J. A. M. A. **142**: 1141, 1950.

A fixed drug eruption following the use of Antabuse for the treatment of chronic alcoholism is reported. Four daily doses of tetraethylthiuram disulfide (Antabuse) and the ingestion of 45 c.c. of whisky on the fourth day, was followed two days later by the appearance of an intensely pruritic erythematous eruption of the thighs, the gluteal, scrotal, lower abdominal, axillary, and cervical regions. The eruption began to clear centrally and was completely gone in eight days. Repetition of the procedure on two subsequent occasions resulted in a lighting up of the identical sites with morphologically similar lesions. Since neither the Antabuse nor the alcohol alone produced the lesions, it is believed that acetaldehyde, which is an in vivo product of the combination of the two agents, was responsible for this fixed eruption. F.

Sensitivity Reactions to Aureomycin. Peck, S. M., and Feldman, F. F.: J. A. M. A. **142**: 1137, 1950.

Three instances of allergic skin reactions due to Aureomycin are reported. Two of the patients were being treated for dermatitis herpetiformis with the antibiotic. Ten days after the beginning of therapy, one developed an erythema multiforme-like eruption and then an urticaria; the second patient developed urticaria on the twentieth day. The third patient developed an eczematoid eruption of the groin and scrotum which began on the eighth day of therapy. Scratch, intradermal, and patch tests performed with Aureomycin yielded negative results. In each case, a recurrence of the dermatitis was precipitated by the readministration of the drug. F.

On Lipstick Dermatitis. Pirila, V.: Acta allergologica **2**: 290, 1949.

Three cases of lipstick dermatitis were found to be due to sensitization to toluene-azo-toluene-azo-beta-naphthol (Sudan IV, Tatan). Cheilitis caused by this azo dye has not been previously reported. Positive patch tests were obtained with both the lipstick and a 1 per cent solution of the dye. These patients also showed positive patch tests with other chemically related dyes. In one case, cheilitis occurred after the lipstick had been applied only five times within a two-month period. In another, cheilitis appeared five days after application of the lipstick for the first time. Previous sensitization could not be ruled out. In the third case, the lipstick had been used for almost two years before the dermatitis developed. In each patient, the skin around the lips was also involved. In one instance where the lipstick was employed as a rouge, dermatitis also appeared on the cheeks. H.

Idiosyncrasy to Ammoniated Mercury. Treatment With 2,3-Dimercaptopropanol (BAL). Williams, B. H., and Beach, W. C.: J. A. M. A. **142**: 1286, 1950.

Ammoniated mercury ointment (3 per cent) was applied to the scalp and forehead of a 3-year-old child on three successive days. Treatment was discontinued when the child developed acute pharyngitis with a high temperature. The fever promptly subsided after sulfonamide therapy and, two days later, the ointment was again applied. Within forty-eight hours an erythematous rash developed over the face and body and the temperature rose. The rash became progressively worse, the fever persisted, and generalized lymphadenopathy was noted. Eosinophilia ranged as high as 23 per cent. The child became progressively worse under symptomatic treatment, and her condition suggested

clinical acrodynia. BAL therapy was instituted and was followed by almost immediate improvement. After seven days of treatment, there was complete recovery. Urinary mercury determinations showed 0.12 mg. of mercury per liter prior to the beginning of BAL treatment and 0.02 mg. of mercury per liter after treatment. F.

Otorhinology and Ophthalmology

Iontophoresis of Pyribenzamine in Allergic Rhinitis. Aaron, T. H.: Canad. M. A. J. **61**: 301, 1949.

Pyribenzamine was administered by nasal iontophoresis to 8 patients suffering from allergic rhinitis. All had previously received antihistaminic drugs orally, without beneficial effects. Relief of symptoms following iontophoresis varied from 3 hours to 1 week, the usual duration of effect being from 1 to 4 days. Saline solution introduced in the same manner was ineffective. The second or third treatment with Pyribenzamine was never so effective as the initial one. K.

Antihistaminic Agents and Ascorbic Acid in the Early Treatment of the Common Cold. Cowan, D. W., and Diehl, H. S.: J. A. M. A. **143**: 421, 1950.

The authors report the results of a well-controlled study on the value of the antihistaminic drugs in the treatment of the common cold. In a series of 367 presumably nonallergic students, 980 colds were treated. There was no indication that these drugs alone or in combination with ascorbic acid had any apparent effect upon the duration or severity of infections of the upper respiratory tract. F.

Miscellaneous Allergies

Anaphylactic Reaction Following Injection of Heparin. Chernoff, A. I.: New England J. Med. **242**: 315, 1950.

A 54-year-old man was admitted to the hospital with the diagnosis of acute myocardial infarction. About 4 hours later, 5 c.c. of sodium heparin solution was administered intravenously. About one minute after the needle was withdrawn, the patient became dyspneic, cyanotic, and perspired profusely. The pulse and blood pressure were unobtainable and the heart sounds could not be heard. Examination of the chest revealed asthmatic breathing. A red macular rash appeared over the entire body. Adrenalin and oxygen were administered and benadryl was started orally. Within 5 minutes, the color and respirations improved. Several hours later, the blood pressure and pulse returned to normal and the rash disappeared. Later, the patient stated that immediately after the injection of heparin, he felt a tingling sensation in his extremities, then an intense burning and itching of his eyes and body, and finally a terrifying inability to breathe. There was no personal or family history of allergy and he had never previously received heparin. The heparin solution was tested for depressor substance, but none was found. About a month later, positive reactions were obtained by scratch and intracutaneous tests with a heparin solution extracted from beef lung and with heparin obtained from pork liver, the type used in this case. Intracutaneous tests with beef, pork, and lamb extracts gave slight but definite reactions. Passive transfer studies yielded positive reactions with all of the above antigens. The same studies repeated on serum obtained 10 months later showed similar results; however, the serum was less reactive than the initial one. Neutralization tests were done but equivocal results were obtained. B. S.

Sensitivity to Vitamin B_{12} Concentrate. Young, W. C., Ulrich, C. W., and Fouts, P. J.: J. A. M. A. **143**: 893, 1950.

A patient with pernicious anemia known to be sensitive to extracts of beef and pork liver was treated with vitamin B_{12} made from streptomycin

broth. After the sixth treatment, he began to experience burning of his throat and itching and swelling about the injection sites. A vitamin B_{12} made from liver was then substituted and was well tolerated. He was then given a second vitamin B_{12} made from streptomycin broth and, after the eleventh injection, he developed marked peripheral circulatory collapse and a severe drop in blood pressure. Recovery occurred after 3 hours of intense symptomatic treatment. A crystalline vitamin B_{12} made from streptomycin broth was then administered without untoward reaction. Intracutaneous tests made with purified liver extracts, with and without added thiamine, and with vitamin B_{12} concentrate from liver gave marked reactions. An erythematous reaction was obtained with vitamin B_{12} made from streptomycin broth. Thiamine produced a slight erythema; crystalline B_{12} and streptomycin gave no reaction. F.

Allergic Reactions in Parenteral Liver Therapy and Vitamin B_{12}. Noren, B.: Acta med. Scandinav. **137**: 48, 1950.

The incidence of allergy to liver in a group of 130 patients with pernicious anemia, all treated parenterally with various brands of liver extract, was investigated. In addition to a careful history, all patients in this group were tested by the scratch and intracutaneous methods with commercial liver preparations, with beef, pork, and horse liver protein, with animal sera, and with vitamin B_{12}.

Twenty-four (18 per cent) of the 130 patients had experienced allergic reactions following parenteral liver injections. Twenty-three of 37 patients, who had reacted positively to intracutaneous tests with liver extracts, manifested allergic symptoms. The organ-specific type of hypersensitivity was found to be more common than the species-specific type. In no case was a positive reaction obtained following intracutaneous testing with vitamin B_{12}. H.

Histology of Lesions Caused by the Sting of Bee. Crewe, W., and Gordon, R. M.: Ann. Trop. Med. **43**: 341, 1949.

Bee sting may affect the individual in one of three ways; the lesions may be caused by the injected poison, by bacterial infection introduced with the venom, or by allergic reactions in previously sensitized individuals. Histologic studies of the lesions produced in guinea pigs are reported. The lesions produced included edema, cellular infiltration, and muscle necrosis. These changes are followed by a walling-off of the damaged tissue by a palisade of inflammatory cells. H.

Anaphylactoid Reaction to Sulfobromophthalein Sodium. Roth, J. L. A.: J. A. M. A. **143**: 802, 1950.

A 38-year-old-man, who had previously had serum sickness following antitetanic serum and urticaria after sulfonamides, was given 430 mg. of sulfobromophthalein intravenously for a liver function test. Immediately after the injection, the patient developed severe inspirational dyspnea and became apprehensive. The skin of the face showed a spotty erythema with circumoral pallor and intense cyanosis. Treatment consisted of epinephrine injections, aminophylline rectally, and oxygen inhalation. Urticaria soon appeared on the abdomen and arms. Further treatment with Demerol, a saline infusion, plasma, and whole blood were necessary before the patient recovered. An ECG, taken during the attack, showed a sinus tachycardia, sharp peaking, and an increase in the amplitude of the T waves. The ECG returned to normal 24 hours after the reaction. A persistent eosinophilia of from 6 to 8 per cent was noted during the subsequent 3 weeks. F.

Unusual Reaction to Penicillin. Felder, S. L., and Felder, L.: J. A. M. A. **143**: 361, 1950.

Urticaria and angioneurotic edema associated with arthralgia was noted in a 53-year-old male 10 days following the first of 4 daily injections of penicillin. All therapeutic measures instituted were of no avail and the condition persisted in severe form. The blood pressure fell from 112/70 to 96/70 and the temperature ranged as high as 103.4° F. Blood chemistry studies revealed many findings suggesting abnormal liver function. A 4 plus precipitin reaction to Trichinella was observed. Electrocardiographic examination showed mild cardiac involvement. On the thirteenth day of the illness, procaine hydrochloride 0.1 per cent in 5 per cent dextrose was given intravenously with dramatic relief. In view of the absence of pain, the myocardial damage was probably of an inflammatory nature. Positive precipitin reactions to Trichinella frequently occur in periarteritis nodosa and various other vascular allergies and are not specific for infestation. F.

Anaphylaxis

Peripheral Vascular Reactions in Anaphylaxis of the Mouse. McMaster, P. D., and Kruse, H.: J. Exper. Med. **89**: 583, 1949.

Mice sensitized with horse serum were given a shocking dose intravenously while their ears were under constant microscopic observation. In from 28 seconds to 7 minutes vascular reactions were noted. First, one or more brief partial contractions of the arteries were noted all along their course. Next, sharply localized contractions appeared. "In highly sensitive animals the localized spasms increased in number and intensity, until, within a minute or two, all arterial vessels were completely constricted . . ." When vascular spasm was delayed a minute or two, the circulation was slow and cells moved in clumps. The veins also contracted, usually only in localized short segments. If the constrictive changes occurred while the carotid blood pressure was normal or slightly elevated, the capillary bed appeared to be dilated only when the veins constricted before the arteries. Otherwise, the capillaries remained patent and were filled with plasma only, since the red cells were prevented from entering by arterial spasm. Apparently, the capillaries were affected only passively by the spasm of arteries and veins. Recovery of circulation in the ears began in from 5 to 20 minutes following the serum injection. Blood started to move again in the arterioles and the ears appeared hyperemic, although the flow of blood was very slow. The systemic blood pressure at this stage was low. Weights just sufficient to occlude circulation were applied to one ear of some mice just prior to the administration of the shock dose of serum. The weights were considered insufficient to affect nerve transmission, yet the typical vascular reactions were prevented. There was no correlation between carotid blood pressure and the vascular reactions of the ears. In many mice, ear circulatory changes were the only evidence of anaphylaxis. The injection of horse serum into nonsensitized mice and the injection of rabbit serum into horse-serum-sensitized mice never produced the above reactions. K.

Effect of ACTH and Cortisone Upon an "Anaphylactoid Reaction." Selye, H.: Canad. M. A. J. **61**: 553, 1949.

Normal, nonsensitized rats exhibit edema of the nose, tongue, and paws, when egg white is administered parenterally. Groups of 10 adrenalectomized rats were treated with desoxycorticosterone acetate (DCA), cortisone and DCA, and cortisone. Untreated rats were employed as controls. Salt was added to the drinking water of the animals. Egg white was injected intraperitoneally 4 days after adrenalectomy. Cyanosis and edema were prominent in animals given DCA and in the controls, but were absent or mild in animals given cortisone with or without DCA. Although the DCA-treated

animals appeared more severely shocked than the controls, they survived, while the untreated controls were all dead by the third hour after injection.

Six rats were then treated with ACTH and 6 served as controls. The administration of egg white caused marked anaphylactoid reactions in all of the controls and barely noticeable responses in only 2 of the ACTH-treated animals. In a third series of experiments, groups of 6 rats each were given ACTH or lyophilized cattle anterior pituitary powder (LAP). One group was untreated and served as the control. On the fifth day of treatment, the injection of egg white produced the most marked anaphylactoid response in the LAP-treated rats, a less marked response in the untreated controls, and a slight transitory reaction in only 2 of the animals pretreated with ACTH. The author emphasizes the opposing actions of DCA and cortisone on thymic hypertrophy, blood sugar, development of posttraumatic shock, formalin arthritis, and hypertension. The intensification of the egg albumin reaction by LAP suggests the possibility that the anterior pituitary "contains additional principles which antagonize the ACTH effect or so modify it that a DCA-like action results." K.

The Role of the "Wax" of the Tubercle Bacillus in Establishing Delayed Hypersensitivity. II. Hypersensitivity to a Protein Antigen, Egg Albumin. Raffel, S., Arnaud, L. E., Dukes, C. D., and Huang, J. S.: J. Exper. Med. **90**: 53, 1949.

Cutaneous reactions to egg albumin were measured at time intervals of from 1 to 48 hours following the intracutaneous injection of egg albumin into several groups of guinea pigs. These groups consisted of controls and animals that had been sensitized by egg albumin with and without the addition of tubercle bacillus wax and with and without emulsification (water-in-oil). The addition of tubercle bacillus wax resulted in delayed (24 to 48 hours) cutaneous responses to egg albumin at a time when skin reactions to simultaneous tests had faded in animals sensitized to egg albumin alone. Antibody titers were not increased in the wax-treated animals and a known adjuvant in the form of water-in-oil emulsion did not affect the appearance of delayed hypersensitivity.

Intracorneal injection of egg albumin followed by histologic examination 48 hours later revealed corneal opacity, thickening, necrosis, and cellular exudation in animals sensitized with albumin plus wax. There was, however, no reaction or only slight changes at the needle puncture site in corneas of animals sensitized with albumin alone. The cornea normally is an avascular tissue; therefore, the Arthus reaction cannot occur and the response obtained is characteristic of tuberculin-type sensitivity. As further confirmation of the induction of tuberculin-type sensitivity to egg albumin under the influence of tubercle bacillus wax, 19 bone marrow explants from animals sensitized to egg albumin alone were cultured and found to be unaffected by the presence of antigen, whereas all of 17 marrow explants from animals sensitized with albumin plus wax were affected as to growth, migration of cells, and cell death, when egg albumin was added.

Pyribenzamine injected either at a distance or incorporated into the skin test dose of albumin failed to alter the immediate skin reactions and was useless in differentiating the Arthus from the tuberculin-type reactions.

Contact-type reactions were not observed following the subcutaneous injection of the mixtures described above. K.

Studies on the Liver Circulation. I. Active Constriction of the Hepatic Venous Tree in Anaphylactic Shock. Maegraith, B. G., Andrews, W. H. H., and Wenyon, C. E. M.: Ann. Trop. Med. **43**: 225, 1949.

Dogs sensitized to horse serum were anesthetized. Their abdomens were opened and from 0.02 to 0.05 ml. of horse serum was injected just under the

surface of the liver. Within 2 minutes the injection site became dark, turgid, and swollen. The reaction was complete within 45 minutes and reinjection into the same site failed to provoke further response, although the injection of horse serum into either the portal vein or one of its branches caused intense congestion of the entire area supplied by the blood vessel, including the previously tested area. Control animals failed to show this response. Rats and guinea pigs treated in the same manner showed similar but less intense responses.

From 0.1 to 0.05 ml. of horse serum was injected directly into the exposed liver of nonsensitized dogs and guinea pigs. Three weeks later, the animals were anesthetized, the abdomens were opened, and the antigen was administered intravenously. Generalized hepatic congestion resulted. It is suggested that, in anaphylactic shock in dogs, guinea pigs, and rats, there is active constriction of the radicles of the hepatic veins and that, under certain circumstances, the smaller radicles of the portal vein may constrict independently. K.

Observations on the Release of Serum "Fibrinolysin" by Specific Antigen, Peptone, and Certain Polysaccharides. Ungar, G., and Mist, S. H.: J. Exper. Med. **90**: 39, 1949.

Sera from egg-sensitized guinea pigs release serum fibrinolysin when egg antigen is added in vitro. Sera from nonsensitized guinea pigs are not similarly affected. Peptone, agar, hyaluronic acid, glycogen, chondroitinsulfuric acid, type-specific pneumococcal polysaccharides, and heparin release the clot-dissolving enzyme from its precursor state in normal guinea-pig serum. No such activating effect was exhibited by thromboplastin, dicoumarin, starch, epinephrine, histamine, or acetylcholine. It is suggested that the highly toxic properties acquired by serum following anaphylaxis or after the introduction of various nonantigenic substances may be due to the presence of a kinase which induces activation of large amounts of fibrinolysin in vivo. The appearance of fibrinolysin when egg antigen is added to egg-sensitive sera in vitro suggests that this process might also occur as part of the mechanism of anaphylactic shock. K.

Isoallergic Encephalomyelitis Produced in Guinea Pigs Via Intramuscular and Intraperitoneal Injection of Antigen. Gazzullo, C. L., and Ferraro, A.: Arch. Path. **48**: 316, 1949.

An emulsion of normal guinea pig brain tissue introduced either intramuscularly or intraperitoneally produced encephalomyelitis in guinea pigs. Histologically, the most prominent lesion was a perivascular inflammatory reaction of the brain and spinal cord. The clinical and pathologic features closely resembled experimentally induced encephalomyelitis in monkeys. Encephalomyelitis may be an allergic reaction since antibrain antibodies have been found in the serum of the monkeys.

This phenomenon may explain postvaccinal encephalitis and the encephalomyelitis which sometimes follows antirabies treatment. J. S.

Pharmacology, Physiology, and Pathology

Treatment of Disseminated Lupus Erythematosus With Cortisone and Adrenocorticotropin. Baehr, G., and Soffer, L. J.: Bull. New York Acad. Med. **26**: 229, 1950.

Five patients with severe disseminated lupus erythematosus were treated with cortisone or ACTH. Four of the patients were women and one was a 15-year-old boy. Each showed a normal response of the adrenal cortex to ACTH prior to the onset of therapy. Within 48 hours after the first dose of either hormone, the patients felt well and the arthralgia improved. Following

4 days of therapy, the temperature fell to normal, cardiac irregularities disappeared, and joint swellings, pericarditis, and pleuritis subsided. Within 10 days, the characteristic erythema subsided, leaving a pigmentation of the affected areas. After 2 or more weeks of therapy, the daily dose was gradually diminished until the daily maintenance requirement was determined. Cessation of hormone therapy resulted in an exacerbation of symptoms within a few days. It was found to be advantageous to switch to ACTH, after the minimum maintenance requirement for cortisone had been determined. The continued suppressive action of cortisone on adrenal cortical function could then be avoided and the patients' own adrenals could aid in maintaining the effect. Despite the clinical improvement, leukopenia, elevated sedimentation rate, and the so-called "L.E." cells in the bone marrow or blood persisted. Disturbed blood electrolyte balance was most commonly seen during the second week of therapy. This complication could not be prevented by a low salt diet and was accentuated by the use of mercurial diuretics. One patient developed epileptiform convulsive seizures on the eighteenth day of cortisone therapy. Another patient developed manic-depressive psychosis with both types of hormones. The authors point out the fact that the dramatic improvement in these cases cannot be interpreted as more than a remission. These potent hormonal agents act in disseminated lupus erythematosus by preventing or arresting the abnormal enzymatic processes in mesenchymal cells initiated by an unknown causative factor, and this action is nonspecific. B. S.

Effects of Pituitary Adrenocorticotropic Hormone (ACTH) Therapy: Electroencephalographic and Neuropsychiatric Changes in Fifteen Patients. Hoefer, P. F. A., and Glaser, G. H.: J. A. M. A. **143**: 620, 1950.

Pre- and post-treatment electroencephalographic and neuropsychiatric studies were made on 15 patients being treated with ACTH. During the course of the hormonal administration the electroencephalographic records of 2 patients remained unchanged, whereas the other 13 showed moderate to severe changes. These changes which usually appeared within 3 to 5 days after the beginning of treatment consisted of (a) a reduction in amplitude, regularity, and continuity of the basic alpha activity, and slowing of the alpha activity, and (b) the appearance of large amounts of slow activity that occurred at random or in bursts. These abnormalities gradually became more pronounced as treatment was continued, but were unrelated to dosage levels or alterations in blood sugar and electrolytes. Ten of the 15 patients showed some neuropsychiatric changes, 2 being of a severe nature. The patients all returned to their pretreatment status after the discontinuance of therapy.

The electroencephalographic changes observed cannot be adequately explained on the basis of the known physiologic alterations induced by ACTH. There are, however, a number of factors such as alterations in dextrose metabolism, interference with acetylcholine cycle, water retention, disturbance in potassium balance, alkalosis, a peculiar toxic effect of the hormone or of excessive adrenocorticol steroids, and hypertension produced by the medication, which in combination may operate to produce these changes. These findings indicate that powerful side reactions may accompany the therapeutic effects of ACTH. F.

Opposite Actions of Thyroid and Adrenal Hormones in Allergic Hypersensitivity. Long, D. A., and Miles, A. A.: Lancet **258**: 492, 1950.

Three groups of guinea pigs were sensitized by intracutaneous injections of tuberculin administered twice weekly. Ten days prior to the first sensitizing injection, one group was started on thyroxine, and the second group was given propylthiouracil. The third group of guinea pigs received no pretreatment, serving as the control. The degree of tuberculin sensitivity was meas-

ured by the diameter of 20-hour reactions to tuberculin injected intracutaneously. Sensitivity increased rapidly in the thyrotoxic animals and slowly in the propylthiouracil-treated and the control groups. Eighteen days after sensitization was begun, one-half of the animals in the propylthiouracil-treated and control groups were given thyroxine. In these animals, sensitivity increased rapidly. The drug was discontinued in one-half of the animals of the thyroxine-treated group. The tuberculin sensitivity diminished in this group to the level of the untreated group.

In another series of experiments, B.C.G.-infected guinea pigs were treated with thyroxine, adrenocorticotropic hormone, or cortisone. Thyroxine-treated animals were found to be more sensitive to tuberculin than the control animals. Two weeks after cessation of thyroxine therapy, the sensitivity in this group was less than in the control group. Tuberculin tests done 2½ hours after a single injection of ACTH showed a diminished sensitivity as compared to controls. Similar results were obtained in sensitized guinea pigs given 3 daily injections of cortisone. However, 2 weeks after the ACTH or cortisone had been given, the animals were found to be more sensitive to tuberculin than the control animals. It is suggested that the diminution of the hormonal effect on tuberculin sensitivity and the swing to the opposite direction within 2 weeks after cessation of administration of the hormone is due to opposition of the thyroid and adrenal cortex. Pathologic studies in the thyroxine-treated guinea pigs revealed enlarged adrenals with pronounced cortical hypertrophy, while the thyroid glands were histologically in the resting stage. Thus, it is postulated that the diminished sensitivity to tuberculin in the thyroxine-treated group after withdrawal of the thyroxine is due to excessive adrenocortical activity. The increased sensitivity in the ACTH-treated group, when that hormone is withdrawn, may be due to overcompensation in thyroid activity. This mechanism may explain the exacerbation of symptoms seen in patients following the discontinuance of the ACTH therapy. B. S.

A Fatal Case of Allergic Dermatitis With Manifestations of Combined Collagen Diseases. Zaino, E. C., and Sharnoff, J. G.: New York State J. Med. **50**: 1261, 1950.

A 70-year-old woman was admitted to a hospital because of a severe dermatitis involving her face, scalp, neck, chest, and arms. About 4 months prior to her admission, she applied "Danderine" shampoo in double strength, having used the material for many years. The following morning, her eyelids were swollen and pruritic. The rash spread to her face, ears, neck, chest, and arms. She was hospitalized at that time for several weeks and treated with Pyribenzamine ointment and x-ray with some improvement. On readmission to a hospital, the eruption was found to be edematous and erythematous with telangiectasia. On the distal ends of her fingers, there were irregular, flat, pink lesions. The eyelids were edematous and there was bilateral conjunctivitis. The blood pressure was 170/100 and the patient ran a low-grade temperature. Moist râles were heard at both lung bases. The electrocardiogram was interpreted as suggesting diffuse, myocardial changes, and a possible posterior wall infarction. The white blood cell differential revealed only 1 or 2 per cent eosinophiles. There was a trace of albumin in the urine with 15 to 20 white blood cells per high-power field. The sedimentation rate was elevated. The total blood protein was low with an inverse albumin-globulin ratio. A skin biopsy showed chronic dermatitis with fibrinoid degeneration of the dermis consistent with acute lupus erythematosus. The patient was given supportive and palliative therapy, but expired about 1 week after admission. At autopsy, the leaflets of the mitral valve were found to be thickened and rolled and small red granules were noted at their edges. Microscopic sections of these areas revealed a marked swelling produced by fibrinoid de-

generation of the collagen fibers. In the heart, fragmentation of myocardial fibers was noted and the arterioles were infiltrated with lymphocytes, plasma cells, and large macrophages. The interstitial stroma also revealed fibrinoid degeneration of the collagen fibers. The perivascular lesions were also found in other organs. The skin showed a diffuse fibrinoid degeneration of the papillary dermis. The reticular layer of the adrenal cortex was extensively necrotic. Bone marrow sections showed a 28 per cent eosinophilia. An invading adenocarcinoma of the gall bladder was an incidental finding. It is suggested that the collagen disease in this case was initiated by an acute allergic dermatitis. B. S.

Induction of Cardiac Lesions, Closely Resembling Those of Rheumatic Fever in Rabbits Following Repeated Skin Infections With Group A Streptococci. Murphy, G. E., and Swift, H. F.: J. Exper. Med. **89**: 687, 1949.

A group of 110 rabbits received intracutaneous injections of live Group A streptococci repeatedly over a period of months. Acute rheumatic-fever-like cardiac lesions were observed in 20 rabbits and myocardial scars or healed arteritis of the rheumatic type were found in 16 animals at autopsy. Adrenal changes were also noted in animals which died spontaneously or those which were sacrified while sick. K.

Excretion of Histamine in Human Urine. Adam, H. M.: Quart. J. Exper. Physiol. **35**: 281, 1950.

A modification of Anrep's method was used to measure free and conjugated histamine in the urine of human subjects. Histamine administered orally to 3 subjects appeared in the urine principally in conjugated form. About one-half of the conjugated histamine appeared in the urine in the first 6 hours, and excretion was nearly complete in 24 hours. Histamine administered intravenously to 3 subjects in amounts sufficient to produce moderate side effects resulted in the appearance of large amounts of free histamine in the urine, and excretion was almost complete in 6 hours. Histamine determinations made on the plasma and the blood cells revealed no increase, even though the specimens were collected during the hypotensive reaction to rapid intravenous infusion. It is concluded that "investigations of the excretion of histamine are more likely to give information about the release of histamine in the body than investigations on venous blood." K.

Eosinophilic Granuloma of the Jejunum: A Hitherto Undescribed Lesion of the Intestines. Polayes, S. H., and Krieger, J. L.: J. A. M. A. **143**: 549, 1950.

A 76-year-old man, hospitalized because of intestinal obstruction and vomiting, was found to have at operation, a large neoplastic-like, obstructing mass in the jejunum. Pathologic examination of the specimen revealed the mass to be composed almost entirely of granulomatous tissue. Within the granuloma there was a reticulum hyperplasia and collagen deposition with massive infiltration of leucocytes. About 96 per cent of the cells were eosinophilic, except in the portion of the lesion involving the muscularis and serosa where the predominant cell was the lymphocyte. In view of the high percentage of eosinophiles, skin tests with various allergens were performed. Positive reactions were obtained only with Oidium and Trichophyton. The etiology of the lesion was not definitely determined, but allergy was strongly suspected. F.

Periarteritis Nodosa—Asthma Bronchiale—Iododerina Tuberosum. Muller, J.: Acta. med. Scandinav. **136**: 378, 1950.

A 28-year-old woman suffering from bronchial asthma was treated with potassium iodide and developed Iododerina tuberosum, recurrent transitory

pulmonary infiltrations, leucocytosis, high eosinophilia, leucocytosis, and polyneuritis. A biopsy revealed periarteritis nodosa. Following the withdrawal of iodides, all the symptoms gradually disappeared and the patient reported that she was well 9 months later.

A second case of Iododerina tuberosum was observed in a 34-year-old woman with bronchial asthma, a high blood eosinophilia, transitory pulmonary infiltrations, leucocytosis, and cardiac failure. This patient went rapidly downhill and died. Post-mortem examination failed to reveal evidence of periarteritis nodosa, but there were vascular changes resembling arteriosclerosis and healed endarteritis. H.

Disseminated Necrotizing Panarteritis (Periarteritis Nodosa). Clinical-Pathologic Report. Winkelman, N. W., and Moore, W. T.: J. Neuropath. & Exper. Neurol. **9**: 60, 1950.

A man, aged 63 years, presented the clinical quardrad of asthma, peripheral neuropathy, eosinophilia in excess of 25 per cent, and a history of having had sulfonamides and penicillin on two occasions. Biopsy confirmed the antemortem diagnosis of necrotizing panarteritis, which was later verified at autopsy. Microscopic studies of the brain revealed involvement of the smaller arteries in the meninges, choroid plexus, and cortex. The most valid etiologic concept of necrotizing panarteritis is that it represents an irreversible allergic process in the blood vessel wall. The collagen in the medium-sized blood vessels is probably the seat of the initial allergic reaction. H.

Administration of Aminophylline (Theophylline Ethylenediamine). Waxler, S. H., and Schack, J. A.: J. A. M. A. **143**: 737, 1950.

Aminophylline blood level studies, expressed in terms of micrograms of theophylline per cent, made at various intervals after the intravenous, intramuscular, oral, and rectal administration of the drug revealed that both the size of the dose and the route of administration influence the concentration and maintenance of the blood levels. One-half hour after the intravenous administration of 0.25 Gm. of aminophylline, there was a mean level of 600 micrograms which was followed by a progressive fall approaching zero at 9 hours. Intramuscular injection of 0.5 Gm. produced a mean level of about 326 micrograms after 1 hour and a sustained level of significant degree which lasted as long as 13 hours. With doses of 0.23 Gm., the levels were 50 per cent lower and persisted for about 8 hours. The ingestion of enteric coated tablets produced markedly variable levels which became appreciable only after a period of 2 hours. Uncoated tablets were more regularly absorbed and quickly produced higher blood levels which persisted for as long as 9 hours. Rectal suppositories were extremely variable in their effect; many individuals failed to show any theophylline blood levels after their instillation while others developed high, long, persisting levels. Since previous work has shown that theophylline does not penetrate the red blood cell membrane, is only slightly bound to protein, and is restricted to the plasma, the therapeutic effect of the drug is probably related to its level in the blood stream. F.

Effect of Tripelennamine Hydrochloride on Acute Inflammation. Weeks, R. E., and Gunnar, R. M.: Arch. Path. **48**: 178, 1949.

The erythema resulting from burns and from the intracutaneous injection of turpentine was reduced following the intravenous injection of tripelennamine in rabbits. The increase of capillary permeability following application of the irritants, as measured by the concentration of dye in the wound after trypan blue was injected intravenously, was not altered by the drug, nor was there any change in the microscopic picture of the resulting acute inflammation. The erythema and the increase in permeability of capillaries which

follows the intracutaneous injection of histamine was also reduced by the drug.

The failure of tripelennamine to alter the increased capillary permeability produced by burns and by injections of turpentine, while completely preventing that produced by the injection of histamine, suggests that substances other than histamine may be responsible for the inflammation produced. J. S.

Miscellaneous

Agranulocytosis After Antihistaminic Therapy: Report of a Case Following the Prolonged Use of Tripelennamine (Pyribenzamine) Hydrochloride. Martland, H. S., and Guck, J. K.: J. A. M. A. **143**: 742, 1950.

After the first few doses of Pyribenzamine, a 60-year-old nurse experienced general malaise, headache, and transient lower abdominal cramps with diarrhea. Therapy was continued and 2 weeks later anorexia and severe lumbosacral aching occurred. By the end of the fifth week, the symptoms had increased insidiously until there was pronounced weakness, anorexia, chills, and fever as high as 104° F. A blood count revealed a leucopenia of 1,950 and 1,300 with almost complete absence of granular elements. Sternal bone marrow smears showed maturation arrest of the granular cells at the myelocyte stage with an increase in lymphoid cells. Withdrawal of Pyribenzamine, treatment with penicillin and aureomycin, and supportive measures resulted in recovery. After the blood picture had returned to normal, the patient was given 50 mg. of Pyribenzamine and promptly experienced a recurrence of symptoms. She was given 3 additional doses on the following day with further aggravation of these symptoms. Serial blood counts at this time revealed a progressive lowering of the total number of white blood cells, but there was no granulocytopenia. F.

Agranulocytosis From Tripelennamine (Pyribenzamine) Hydrochloride. Hilker, A. W.: J. A. M. A. **143**: 741, 1950.

After 7 weeks of tripelennamine therapy, a 39-year-old nurse began to experience marked weakness. Physical examination performed at the end of the eighth week was negative except for the white blood cell count which was 1,700 with only 6 neutrophiles. No other medications had been taken during the preceding 8 weeks. Withdrawal of Pyribenzamine and treatment with penicillin was followed by rapid recovery. F.

Toxic Psychosis Due to Prophenpyridamine (Trimeton): Report of a Case. Yapalater, A. R., and Rockwell, F. V.: J. A. M. A. **143**: 428, 1950.

A psychotic reaction resembling schizophrenia occurred in an 18-year-old male who had been in excellent health except for an allergic rhinitis. For 2 months prior to the onset of the psychosis, he had taken 25 mg. of Trimeton 3 times a day. The patient was institutionalized with a diagnosis of schizophrenia. On the eighth day of hospitalization and after the Trimeton had been discontinued, he began to show marked improvement and within a short time had completely recovered. Because it was suspected that the condition may have been a toxic reaction to the antihistaminic, trial doses of Trimeton and Chlortrimeton were given for 3 days and electroencephalographic studies were then made. Normal readings were obtained after the Trimeton, but definitely abnormal readings were noted after the Chlortrimeton. F.

Anemia Following Use of Antihistaminic Drugs. Crumbley, J. J., Jr.: J. A. M. A. **143**: 726, 1950.

Three cases of hemolytic anemia apparently resulting from the ingestion of Benadryl and Pyribenzamine were observed. One patient had taken the

antihistaminic for a period of 10 months, another for 14 months, and a third for only 2 months before the anemia was discovered. Treatment with liver and iron, in the first case, and with iron alone in the second failed to produce significant clinical improvement. Withdrawal of the antihistaminics was followed by a return to a normal blood picture in each of the three cases. F.

Serological Studies in Rheumatic Fever. I. The "Phase" Reaction and the Detection of Autoantibodies in the Rheumatic State. Fischel, E. E., and Pauli, R. H.: J. Exper. Med. **89**: 669, 1949.

It was previously reported that a substance called a precipitogen appeared in the serum of a rheumatic subject, following a sore throat (Phase I) or during the latent period (Phase II). This substance, when mixed with serum obtained during the period of rheumatic fever activity (Phase III) resulted in the formation of a precipitate. Serum taken in Phase I failed to show precipitogen in those cases where active rheumatic fever did not subsequently develop. This study was repeated and amplified by the inclusion of carmine dye and collodion particle technique. "No correlation was found between the occurrence of precipitates and the occurrence of any clinical episode, either sore throat or rheumatic fever. Furthermore, repeated tests failed to give reproducible results." It is suggested that the phase phenomenon is related to colloidal abnormality of the serum rather than to a specific antigen-antibody reaction. Attempts were also made to demonstrate autoantibodies for liver tissue in rheumatic fever serum. "No evidence of complement fixation was found in dilutions of serum and of tissue extract which were not anticomplementary alone." Efforts were also made to repeat studies on autoantibodies to other tissues, using the collodion agglutination technique. No specific autoantibodies to human tissue extracts were demonstrable. "Variable results were noted with the same test sera on different occasions, and positive reactions with control tissues and control sera were observed." In some instances, bacterial contamination of tissues, such as tonsils, seemed to be responsible for agglutination. K.

A Misconception Concerning the Rh Factor and the Interruption of Pregnancy. Kendig, E. L.: Am. J. Dis. Child. **76**: 689, 1948.

Two instances are detailed of pregnancy in multigravid Rh negative women. The husbands in both cases were Rh positive. During pregnancy, there was a rising titer of anti-Rh antibodies. Both women were delivered of normal Rh negative babies. This seems to indicate that nonspecific anamnestic antibody responses can confuse the serologic picture. A warning is issued against interrupting pregnancy because the anti-Rh antibody titer increases. K.

Localization of Antigen in Tissue Cells. II. Improvements in a Method for the Detection of Antigen by Means of Fluorescent Antibody. Coons, A. H., and Kaplan, M. H.: J. Exper. Med. **91**: 1, 1950.

Fluorescein isocyanate was conjugated with therapeutic antipneumococcal rabbit serum, type III. Frozen sections from normal, immunized, or infected animals were mounted on glass slides and a drop of conjugate was then added to the preparation. After 20 or 30 minutes, the slide was rinsed, dried, and examined with a fluorescent microscope. The antibody was precipitated by contact with antigen and produced a brilliant green fluorescent area which contrasted with the surrounding blue fluorescent tissue. Careful controls were necessary since nonspecific staining can occur. K.

Immunochemical Studies on Tobacco Mosaic Virus. VI. The Effect of Papain on the Antibody-Antigen Complex. Malkiel, S.: J. Immunol. **64**: 197, 1950.

The precipitate formed by adding tobacco mosaic virus (TMV) to an excess of rabbit antiserum was digested with papain. The TMV thus isolated from the antigen-antibody complex behaved physically the same as the intact virus. It contained methionine and histidine, neither of which is present in native TMV, but is present in antibody globulin. The residual antibody attached to the papain-isolated TMV reacted with anti-rabbit-globulin serum and reduced the infectivity of the isolated TMV. I. GLAZER.

The Isolation of Three Different Proteins and Two Polysaccharides From Tuberculin by Alcohol Fractionation. Their Chemical and Biological Properties. Seibert, F. B.: Am. Rev. Tuberc. **59**: 86, 1949.

Two polysaccharides (I and II) and three protein fractions (A, B, C) may be regularly isolated from raw unheated tuberculin by chemical processes which are described in detail. Another protein component (D) was found in 5-week-old cultures but not in older ones. The relative amounts of the above components varied with different strains of tubercle bacilli. Electrophoretic and spectroscopic patterns are presented. When sensitive humans or guinea pigs were tested with the protein fractions, each so adjusted as to have the same nitrogen content, protein A produced the greatest cutaneous response, protein B gave intermediate reactions, while the protein C fraction was least reactive. The electrophoretic mobilities of these proteins were least for A, intermediate for B, and greatest for C. The polysaccharides failed to elicit skin responses. K.

Studies of Pulmonary Findings and Antigen Sensitivity Among Student Nurses. V. Doubtful Reactions to Tuberculin and Histoplasmin. Palmer, C. E., and Petersen, U. S.: U. S. Pub. Health Rep. **65**: 1, 1950.

Statistical methods, developed as an approach to the interpretation of cutaneous reactions to tuberculin and histoplasmin, are presented. Examination of the data obtained in previous studies by these methods revealed that the prevalence of nonspecific reactions followed a geographic pattern quite different from that of specific reactions. The authors suggest that many positive tuberculin reactions, particularly those elicited with the high dosages now in common use, are actually nonspecific. Such reactions most probably represent cross-reactions produced by infection with other alcohol-acid-fast organisms. H.

The Treatment of Pruritis From Chicken Pox With Pyribenzamine. Silverman, L. B.: J. Pediat. **35**: 442, 1949.

Pyribenzamine afforded prompt relief in two cases of severe pruritis due to chicken pox. Thereafter, Pyribenzamine was routinely prescribed as part of the symptomatic treatment for all cases of chicken pox. As a result, there were no complaints of itching and the incidence of secondary skin infections was reduced. No appreciable side effects from the drug were noted. J. S.